

OFFICE OF NEW ANIMAL DRUG EVALUATION
REVIEWERS' CHAPTER

**ENVIRONMENTAL REVIEW: EVALUATING CLAIMS OF CATEGORICAL
EXCLUSION FOR ACTIONS RELATING TO NEW ANIMAL DRUGS**

- I. The Requirement for Environmental Review
- II. Administrative Responsibility for Environmental Review
- III. Determining whether an Action Qualifies for a Categorical Exclusion
- IV. Extraordinary Circumstances
- V. Categorical Exclusion of Investigations Under an INAD
- VI. Categorical Exclusion of an Approval of a New Animal Drug
- VII. Categorical Exclusion of Suitability Petitions
- VIII. Reference

I. THE REQUIREMENT FOR ENVIRONMENTAL REVIEW

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions and to ensure that the interested and affected public is informed of environmental analyses. The Council on Environmental Quality (CEQ) is responsible for overseeing Federal efforts to comply with NEPA. Both CEQ and the Food and Drug Administration (FDA) have issued regulations governing agency obligations and responsibilities under NEPA. CEQ's regulations implementing the procedural requirements of NEPA can be found at 40 CFR Parts 1500-1508 and FDA's NEPA policies and procedures can be found at 21 CFR Part 25.

Under FDA's regulations, 21 CFR 25.15(a), all applications or petitions requesting agency action require the submission of an environmental assessment (EA) or a claim of categorical exclusion. CEQ and FDA regulations, 40 CFR 1508.4 and 21 CFR 25.5(a)(1), respectively, define "categorical exclusion" to mean a category of actions which have been found by procedures adopted by the Federal agency not to individually or cumulatively have a significant effect on the human environment and for which, therefore, neither an EA nor an environmental impact statement is required. There may be extraordinary circumstances under which an action that would ordinarily be excluded may have a significant environmental effect. A claim of categorical exclusion must include a citation to the particular categorical exclusion that is claimed, a statement of compliance

with the categorical exclusion criteria, and a statement that to the applicant's knowledge, no extraordinary circumstances exist (21 CFR 25.15(a), (d)).

II. ADMINISTRATIVE RESPONSIBILITY FOR ENVIRONMENTAL REVIEW

The primary reviewer (HFV-101, 110, 120, 130, or 140) is responsible for making sure that an applicant has submitted an EA or a claim of categorical exclusion. In accordance with 21 CFR 25.15(a), failure of the applicant to submit an EA or claim of categorical exclusion is grounds for FDA to refuse to file or approve an application or petition.

If an applicant claims a categorical exclusion, it is the responsibility of the primary reviewer to determine whether the action being requested falls within the categorical exclusion cited by an applicant and, if the action falls within the categorical exclusion, whether the sponsor has certified that no extraordinary circumstances exist. If after consultation with the team leader, the primary reviewer is (1) uncertain whether an action falls within the categorical exclusion cited by the sponsor, (2) finds on the face of the submission that there is reason to question whether there are extraordinary circumstances that make it necessary to conduct further environmental review, or (3) is aware of extraordinary circumstances, the primary reviewer should consult with the Environmental Assessment Team in person or via email. Documentation of the consultation with the Environmental Assessment Team should be added to the file by the reviewer, e.g., by incorporation of a memorandum or email in the administrative file, inclusion of a notation of the consultation in the document summary, or other appropriate documentation. If an action is not categorically excluded, an EA should be provided by the sponsor and reviewed by the Environmental Assessment Team.

III. DETERMINING WHETHER AN ACTION QUALIFIES FOR A CATEGORICAL EXCLUSION

The first step in determining whether an action qualifies for a categorical exclusion is to see whether the action falls within a categorical exclusion defined by statute or regulation. The primary reviewer should refer to 21 CFR 25.33 for the list of categorical exclusions for classes of actions relating to animal drugs. If an action falls within a categorical exclusion, the primary reviewer should then confirm that the claim for categorical exclusion, consistent with 21 CFR 25.15(d),

includes a statement that to the applicant's knowledge no extraordinary circumstances exist. If the action qualifies for categorical exclusion under more than one type of action, the primary reviewer should select the single most appropriate categorical exclusion that best fits the action. If there are any questions regarding the best fit, the primary reviewer should contact the Environmental Assessment Team.

Types of animal drug actions that generally qualify for categorical exclusion include:

- Actions on applications that do not increase the use of the drug. 21 CFR 25.33(a). "Increased Use" is defined at 21 CFR 25.5(b)(4).
- Actions on applications for substances that occur naturally in the environment such as electrolytes, peptides, proteins, or vitamins. 21 CFR 25.33(c).
- Actions on applications for drugs intended for use only in non-food animals. 21 CFR 25.33(d)(1).
- Actions on applications for anesthetics, both local and general, that are individually administered to animals. 21 CFR 25.33(d)(2).
- Actions on applications for nonsystemic topical and ophthalmic animal drugs. 21 CFR 25.33(d)(3).
- Actions on applications for new animal drugs intended for use in minor species reared and treated similarly to a major species for which an EA already exists. 21 CFR 25.33(d)(4).
- Actions on applications for new animal drugs intended for use under prescription or veterinarian's order for therapeutic use in terrestrial species. 21 CFR 25.33(d)(5).

The VICH¹ document (Guidance for Industry # 89, ENVIRONMENTAL IMPACT ASSESSMENT (EIA) FOR VETERINARY MEDICINAL PRODUCTS (VMPS)-PHASE I) regarding environmental review provides further guidance regarding how to determine when actions qualify for categorical exclusion and when extraordinary circumstances may exist.

IV. EXTRAORDINARY CIRCUMSTANCES

In accordance with 21 CFR 25.21, FDA must require at least an EA for any specific action that ordinarily would be categorically excluded if extraordinary circumstances indicate that the specific proposed action may significantly affect

¹ VICH stands for International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products. The VICH works to develop a unified standard for the mutual acceptance of data by regulatory authorities responsible for registering veterinary medicinal products.

the quality of the human environment. Extraordinary circumstances include, but are not limited to:

- Actions for which available data establish that, at the expected level of exposure, there is potential for serious harm to the environment (21 CFR 25.21(a)).
- Actions that adversely affect endangered or threatened flora or fauna (21 CFR 25.21(b)).
- Actions relating to new animal drugs intended for use in food animals in a terrestrial environment if the predicted environmental concentration in soil (with or without mitigation) is equal to or greater than 100 micrograms per kilogram.
- Actions relating to new animal drugs that are intended for use in food animals if they are new endo- and/or ectoparasiticides.

40 CFR 1508.27, which describes when an effect is “significant,” provides further examples of extraordinary circumstances under which an environmental assessment may be required for an action that would ordinarily be categorically excluded.

V. CATEGORICAL EXCLUSION OF INVESTIGATIONS UNDER AN INAD

Actions relating to investigations conducted after an investigational new animal drug file (INAD) is established are generally categorically excluded under 21 CFR 25.33(e). It is likely, however, that INADs for aquatic species and investigations with recombinant gene technology will need to be considered by the Environmental Assessment Team. Categorical exclusions ordinarily cover all investigations under the INAD and are not just for individual investigations under the INAD. Once an INAD has been categorically excluded, no further documentation is ordinarily needed. However, if at any time during the INAD, the primary reviewer believes extraordinary circumstances exist which call into question the categorical exclusion for the INAD, the primary reviewer should consult with the Environmental Assessment Team. If the sponsor did not claim an exclusion for investigations under an INAD, the reviewer should contact the sponsor by phone or letter and request that the sponsor make a claim for categorical exclusion or provide an EA as follows:

Your submission did not claim a categorical exclusion from the requirement to prepare an environmental assessment (EA) or include an EA as required in 21 CFR 25.15(a). If you feel that a categorical exclusion is appropriate, please claim an exclusion under 21 CFR 25.33(e). If you make such a claim, you must, in accordance with 21 CFR 25.15(a), be able to state that to your knowledge no

extraordinary circumstances, 21 CFR 25.21, exist which may significantly affect the human environment. If you do not feel a claim for an exclusion is supportable, please prepare an EA and forward it to FDA for review.

(If the sponsor does not claim a categorical exclusion, or submit an EA, then further actions (e.g., authorization letter) on that INAD may be suspended.)

If the reviewer finds that investigations under an INAD are categorically excluded, the letter to the sponsor should include the following language:

Your claim for the investigational use of [drug] for [proposed intended uses if not stated in a prior paragraph] falls within the categorical exclusion in 21 CFR 25.33(e). Your submission states that to your knowledge, no extraordinary circumstances exist which may significantly affect the human environment. Therefore, neither an environmental assessment (EA) nor an environmental impact statement is required. This categorical exclusion from preparation of an EA and an Environmental Impact Statement does not relieve you of the responsibility for determining and meeting all Federal, State, and local environmental and occupational laws and regulations that apply to the manufacturing, use, and disposal of the investigational drugs.

VI. CATEGORICAL EXCLUSION OF AN APPROVAL OF A NEW ANIMAL DRUG

Because 21 CFR 25.15 requires that all applications requesting agency action include the submission of a claim for categorical exclusion or an EA, any NADA, supplemental application, including a supplemental application for manufacturing changes, or abbreviated new animal drug application must include a claim for categorical exclusion or an EA. These may be submitted for review under the phased review process or as part of a New Animal Drug Application (NADA).

If a claim for categorical exclusion is submitted under the phased review process and the primary reviewer finds that the approval of the new animal drug for the proposed uses and conditions of use falls within the claimed categorical exclusion, the primary reviewer should prepare a technical section complete letter (to be filed under an INAD) and include the following language:

[By letter dated,] you claimed a categorical exclusion under 21 CFR 25.___ for the approval of [product] [for intended uses and conditions of use if not previously stated]. Furthermore, your submission states that to your knowledge, no extraordinary circumstances exist which may significantly affect the human environment.

CENTER FOR VETERINARY MEDICINE
PROGRAM POLICY AND PROCEDURES MANUAL GUIDE 1243.7220

We agree that the approval of [drug] for [intended uses and conditions of use] falls within the categorical exclusion under 21 CFR ___ and that no extraordinary circumstances exist. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Based on the information in this submission and INAD ___, the Division of [name of Division] considers the environmental technical section to be complete for the purpose of recommending approval of a new animal drug application (NADA). A final decision on the approval of the application will be made when all the data for all technical sections are viewed as a whole and it is determined that the information contained in and referenced by the application supports approval. If there are changes in the product (e.g., indication, dosage, duration of use) before the NADA is submitted, please contact the primary reviewer immediately to determine if the categorical exclusion remains appropriate for the action.

Please include a copy of this letter in your NADA submission at Section 10 (FDA Form 356V), Environmental Assessment. By signing the 356V, you certify that the conditions of the categorical exclusion are still applicable at the time of your NADA submission.

If a claim for categorical exclusion is submitted under the phased review process or as part of the NADA and the primary reviewer finds that the claim is inappropriate, the reviewer should prepare an incomplete letter and include the following language:

We have reviewed your claim for categorical exclusion and find that it is inappropriate because [the proposed action does not fall within the claimed categorical exclusion] or [there are extraordinary circumstances]. [Specific reason(s) for denying the categorical exclusion should be given and the letter should specify what environmental information is being requested by the Environmental Assessment Team or direct the sponsor to meet with the Environmental Assessment Team].

A sponsor should be encouraged to submit a claim for categorical exclusion during phased review. If a claim for categorical exclusion is initially submitted as part of the NADA and an EA is then required, significant delays in approval may

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occur. If the primary reviewer finds that the approval of the new animal drug for the proposed uses and conditions of use falls within the claimed categorical exclusion, the approval package and the approval regulation² should cite the categorical exclusion and state that FDA has found that the action qualified for categorical exclusion and no extraordinary circumstances exist.

The Federal Register notice announcing the approval of a new animal drug that qualifies for categorical exclusion should include the following statements:

The agency has determined under 21 CFR 25.33(d) (insert number of applicable exclusion) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. CATEGORICAL EXCLUSION OF SUITABILITY PETITIONS

Actions relating to suitability petitions are generally categorically excluded under 21 CFR 25.30(h).

VIII. REFERENCE

Program Policy & Procedures Manual Guide 1243.4080, Technical Section
Complete Letters

² One purpose of the National Environmental Policy Act is to insure that environmental information is available to public officials and citizens. If environmental information is not included in the approval regulation, FDA should use some other mechanism such as the FOI summary to make the information available to the public.